

General

Guideline Title

Guidelines of care for the management of atopic dermatitis. Section 4. Prevention of disease flares and use of adjunctive therapies and approaches.

Bibliographic Source(s)

Sidbury R, Tom WL, Bergman JN, Cooper KD, Silverman RA, Berger TG, Chamlin SL, Cohen DE, Cordoro KM, Davis DM, Feldman SR, Hanifin JM, Krol A, Margolis DJ, Paller AS, Schwarzenberger K, Simpson EL, Williams HC, Elmets CA, Block J, Harrod CG, Smith Begolka W, Eichenfield LF. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. J Am Acad Dermatol. 2014 Dec;71(6):1218-33. [157 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Hanifin JM, Cooper KD, Ho VC, Kang S, Krafchik BR, Margolis DJ, Schachner LA, Sidbury R, Whitmore SE, Sieck CK, Van Voorhees AS. Guidelines of care for atopic dermatitis. J Am Acad Dermatol. 2004 Mar;50(3):391-404. [212 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Level of evidence grades (I-III) and strength of recommendations (A-C) are defined at the end of the "Major Recommendations" field.

Note from the National Guideline Clearinghouse (NGC): Recommendations on atopic dermatitis (AD) treatment and management are subdivided into 4 sections given the significant breadth of the topic. This document is the final in the series of 4 publications and discusses the management and control of AD flares using topical modalities and the utility and timing of allergen testing and avoidance. Also discussed is the use of adjunctive therapies and approaches, such as environmental, dietary, and educational interventions, in addition to complementary therapies.

Recommendation for Prevention of Flares of Atopic Dermatitis

Continued use of either topical corticosteroids (1 to 2 times/week) or topical calcineurin inhibitors (2 to 3 times/week) after disease stabilization, to previously involved skin, is recommended to reduce subsequent flares or relapses.

Strength of Recommendations for the Use of Topical Therapies for Flare Prevention and for Adjunctive and Complementary Interventions for the Treatment of Atopic Dermatitis

Therapy/Intervention	Strength of Recommendation	Level of Evidence	References
Proactive use of topical corticosteroids	A	I	Hanifin, Gupta, & Rajagopalan, 2002; Berth-Jones et al., 2003; Glazenburg et al., 2009; Peserico et al., 2008; Van der Meer et al., 1999; Schmitt et al., 2011
Proactive use of topical calcineurin inhibitors	A	I	Breneman et al., 2008; Thaci et al., 2010; Wollenberg et al., 2008
Structured education programs	A	I	Grillo et al., 2006; Ricci et al., 2009; Staab et al., 2006; Lambert et al., 2011; Kupfer et al., 2010; Staab et al., 2002
Video interventions	B	II	Niebel et al., 2000; Armstrong et al., 2011
Eczema workshops, nurse-led programs	B	II	Cork et al., 2003; Gradwell et al., 2002; Moore et al., 2006; Moore et al., 2009; Broberg et al., 1990; Chinn, Poyner, & Sibley, 2002
Elicit history of environmental and food allergies	B	II	Boyce et al., 2010; Oranje et al., 1994; Sicherer & Sampson, 1999; Niggemann, Riebel, & Wahn, 2000
Allergy assessment if positive history elicited	B	II	Boyce et al., 2010; Sampson & Albergo, 1984; Lemon-Mule et al., 2008; Breuer et al., 2004; Tuft & Heck, 1952; Darsow et al., 2005; Niggemann, Riebel, & Wahn, 2000; Sampson, 1999
Patch testing for allergic contact dermatitis (ACD)	B	II	Jacob et al., 2010; Lever & Forsyth, 1992; Mailhol et al., 2009; Jacob, Burk, & Connelly, 2008; Moustafa et al., 2011
Against food elimination based on allergy tests only	B	II	Bath-Hextall, Delamere, & Williams, 2008; Niggemann et al., 2001; Uenishi et al., 2008; Norrman et al., 2005; Bath-Hextall, Delamere, & Williams, 2009; Mabin, Sykes, & David, 1995
Avoidance if true immunoglobulin E (IgE)-mediated allergy	A	I	Boyce et al., 2010; Fleischer et al., 2011
Against routine use of probiotics/prebiotics for treatment of established atopic dermatitis (AD)	B	II	Viljanen, et al., 2005; Boyle et al., 2009; Hattori et al., 2003; Passeron et al., 2006; van der Aa et al., 2010
Insufficient evidence to recommend fish oils, evening primrose oil, borage oil, multivitamin supplements, zinc, vitamin D, vitamin E, and vitamins B ₁₂ and B ₆	B	II	Mayser et al., 2002; Soyland et al., 1994; van Gool, Zeegers, & Thijis, 2004; Bamford, Gibson, & Renier, 1985; Berth-Jones & Graham-Brown, 1993; Morse et al., 1989; Senapati, Banerjee, & Gangopadhyay, 2008; Skogh, 1986; Henz et al., 1999; Takwale et al., 2003; Bath-Hextall et al., 2012; Ewing et al., 1991; Javanbakht et al., 2011; Sidbury et al., 2008; Tsourelis-Nikita et al., 2002; Mabin et al., 1995
Against routine use of house dust mite covers	B	II	Gutgesell et al., 2001; Friedmann & Tan, 1998; Oosting et al., 2002; Tsitoura et al., 2002; Holm et al., 2001
Against specific laundering techniques or specific products	C	III	Andersen et al., 1998; Kiriyaama, Sugiura, & Uehara, 2003
Insufficient evidence to recommend specialized clothing fabrics	B	II	Ricci et al., 2004; Senti et al., 2006; Vlachou, Thomas, & Williams, 2009
Against sublingual and injectional immunotherapy for the general AD population	B	II	Cadario et al., 2007; Pajno et al., 2007; Nahm et al., 2008; Bussmann et al., 2007; Werfel et al., 2006; Leroy et al., 1991; Leroy et al., "Treatment of atopic," 1992; Leroy et al., "Allergen-antibody," 1992; Glover & Atherton, 1992
Insufficient evidence to recommend Chinese herbal therapy	C	III	Zhang et al., 2004; Hon, Chan, & Leung, 2011; Keane et al., 1999
Insufficient evidence to recommend massage therapy	B	II	Schachner et al., 1998; Anderson, Lis-Balchin, & Kirk-Smith, 2000
Insufficient evidence to recommend aromatherapy,	B	II and III	Itamura, 2007; Lee et al., 2012

Therapy/Intervention naturopathy, hypnotherapy, acupressure, or autologous blood injections	Strength of Recommendation	Level of Evidence	References
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Recommendations for Educational Interventions for Atopic Dermatitis

- Educational programs (i.e., training programs and "eczema schools") are recommended as an adjunct to the conventional therapy of AD.
- Video interventions can be recommended as an adjunct to conventional therapy.
- Eczema workshops and nurse-led programs may be useful as an adjunct to conventional therapy.

Recommendations for Testing for Coexisting Allergic Disease

- AD patients have an increased rate of environmental and food allergies, and physicians should assess for these conditions during history taking. If significant concerns for allergy are identified (i.e., hives, urticaria, etc.) assessment can be undertaken. Allergy testing independent of history is not recommended.
- Patch testing should be considered in patients with AD who have persistent/recalcitrant disease and/or a history or physical examination findings consistent with allergic contact dermatitis.

Recommendations for Other Adjunctive and Complementary Interventions for the Treatment of Atopic Dermatitis

- Food elimination diets based solely on the findings of food allergy test results are not recommended for the management of AD.
- If a patient has a true immunoglobulin E-mediated allergy, he or she should practice avoidance to prevent potential serious health sequelae.
- Children <5 years of age with moderate to severe AD should be considered for food allergy evaluation for milk, egg, peanut, wheat, and soy if at least 1 of the following is met: (A) persistent AD in spite of optimized treatment or (B) having a reliable history of immediate reaction after ingestion of a specific food.
- The use of probiotics/prebiotics for the treatment of patients with established AD is not recommended because of inconsistent evidence.
- There is inconsistent to no evidence to recommend the use of fish oils, evening primrose oil, borage oil, multivitamin supplements, zinc, vitamin D, vitamin E, and vitamins B₁₂ and B₆ for the treatment of AD.
- There is limited evidence to support the routine use of house dust mite covers to treat patients with AD who are sensitized to dust mites.
- The use of specific laundering techniques, such as double rinsing, detergents, or other laundry products cannot be recommended for AD treatment because of the lack of clinical studies.
- There is limited evidence to support the use of specialized clothing fabrics in the treatment of AD.
- In the general AD population, sublingual immunotherapy and injection immunotherapy are not recommended for the treatment of AD because of the small number of studies and conflicting conclusions.
- Chinese herbal therapy and massage therapy have insufficient evidence for recommendation for AD treatment.
- The use of aromatherapy, naturopathy, hypnotherapy, acupressure, or autologous blood injections cannot be recommended for the treatment of AD at this time because of insufficient evidence.

Definitions

Level of Evidence

- I. Good-quality *patient-oriented evidence* (i.e., evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life)
- II. Limited-quality patient-oriented evidence
- III. Other evidence, including consensus guidelines, opinion, case studies, or *disease-oriented evidence* (i.e., evidence measuring intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes)

Grade of Recommendation

- A. Recommendation based on consistent and good-quality patient-oriented evidence
- B. Recommendation based on inconsistent or limited-quality patient-oriented evidence
- C. Recommendation based on consensus, opinion, case studies, or disease-oriented evidence

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Atopic dermatitis (AD; atopic eczema)

Note: The treatment of other forms of eczematous dermatitis is outside the scope of this document.

Guideline Category

Management

Prevention

Treatment

Clinical Specialty

Allergy and Immunology

Dermatology

Family Practice

Internal Medicine

Pediatrics

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To address the management of pediatric and adult atopic dermatitis (AD; atopic eczema) of all severities

Target Population

Pediatric and adult patients with atopic dermatitis (AD; atopic eczema)

Interventions and Practices Considered

1. Topical corticosteroids or topical calcineurin inhibitors
2. Education programs
3. Video interventions
4. Eczema workshops, nurse-led programs
5. Patient history of environmental and food allergies and assessment if significant concerns are identified (testing independent of history is not recommended)

6. Patch testing for allergic contact dermatitis
7. Food allergy evaluation (milk, egg, peanut, wheat, and soy) in children <5 years of age with moderate to severe atopic dermatitis (AD) if indicated
8. Avoidance if true immunoglobulin E (IgE)-mediated allergy

Note: The following interventions were considered but not recommended or there was limited evidence to support a recommendation:

- Food elimination based on allergy tests only
- Probiotics/prebiotics
- Fish oils, evening primrose oil, borage oil, multivitamin supplements, zinc, vitamin D, vitamin E, vitamins B12 and B6
- House dust mite covers
- Specific laundering techniques
- Specialized clothing fabrics
- Sublingual immunotherapy and injection immunotherapy
- Chinese herbal therapy and massage therapy
- Acupuncture, naturopathy, hypnotherapy, acupressure, or autologous blood injections

Major Outcomes Considered

- Prevention of flares
- Utility of screening for allergens
- Effectiveness of educational programs
- Effectiveness of dietary interventions
- Effectiveness of environmental modifications, allergen-based interventions and complementary therapies

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

An evidence-based model was used, and evidence was obtained using a search of the PubMed and the Global Resources for Eczema Trials databases from November 2003 through November 2012 for clinical questions addressed in the previous version of this guideline published in 2004, and from 1960 to 2012 for all newly identified clinical questions determined by the work group to be of importance to clinical care. Searches were prospectively limited to publications in the English language. Medical Subject Headings terms used in various combinations in the literature search included: atopic dermatitis, atopic eczema, surveillance, long-term management, short-term management, short-term care, long-term care, flare progression, relapse, patient follow-up, patient compliance, contact allergen, contact allergy screen, contact allergy test, desensitization, allergen antibody, anti-allergen, antibody, dust mites, environmental, food allergy, irritant avoidance, detergent, clothing, diet, supplement, food introduction, oil, pyridoxine, vitamin, zinc, education, complementary, alternative, herb, supplement, homeopathy, massage, acupuncture, and Chinese medicine.

A total of 2062 abstracts were initially assessed for possible inclusion. After the removal of duplicate data, 287 were retained for final review based on relevancy and the highest level of available evidence for the outlined clinical questions.

The Academy's previously published guidelines on atopic dermatitis (AD) were evaluated, as were other current published guidelines on AD.

Number of Source Documents

A total of 287 publications were retained for final review

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence was graded using a 3-point scale based on the quality of methodology and the overall focus of the study as follows:

- I. Good-quality *patient-oriented evidence* (i.e., evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life)
- II. Limited-quality patient-oriented evidence
- III. Other evidence, including consensus guidelines, opinion, case studies, or *disease-oriented evidence* (i.e., evidence measuring intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes)

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence tables were generated for included studies and used by the work group in developing recommendations.

The available evidence was evaluated using a unified system called the Strength of Recommendation Taxonomy (SORT) developed by editors of the US family medicine and primary care journals (i.e., *American Family Physician*, *Family Medicine*, *Journal of Family Practice*, and *BMJ USA*). Evidence was graded using a 3-point scale based on the quality of methodology (e.g., randomized control trial, case control, prospective/retrospective cohort, case series, etc.) and the overall focus of the study (i.e., diagnosis, treatment/prevention/screening, or prognosis) (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

A work group of recognized atopic dermatitis (AD) experts was convened to determine the audience and scope of the guideline, and to identify important clinical questions in the management of flare progression and the use of adjunctive therapies and approaches.

Clinical questions used to structure the evidence review for the prevention of disease flares and use of adjunctive therapies and approaches:

- What are the most effective approaches to preventing flares in patients with AD?
- What types of educational interventions are used in patients with atopic dermatitis to improve patient outcome, and are they effective?
- What is the utility of screening for allergens on the course of AD and what are the suggested testing methods?
- What is the effectiveness of dietary interventions, such as dietary restriction based on food allergy and sensitization testing, and the use of supplements, such as evening primrose oil, borage oil, fish oil, pyridoxine, vitamin E, multivitamins, and zinc for the treatment of AD?
- What environmental modifications, such as house dust mite reduction, choice of clothing, irritant avoidance, and use of detergents can be implemented to influence the course of AD?
- What is the effect of allergen-based interventions (e.g., desensitization injections, allergen-antibody complexes of house dust mites) on the course of AD?
- What is the effectiveness of complementary therapies, such as Chinese herbs and other supplements, homeopathy, and massage therapy for the treatment of AD?

Clinical recommendations were developed based on the best available evidence. In those situations where documented evidence-based data were not available, the work group used expert opinion to generate their clinical recommendations.

Rating Scheme for the Strength of the Recommendations

Clinical recommendations were developed based on the best available evidence. These are ranked as follows:

- A. Recommendation based on consistent and good-quality patient-oriented evidence.
- B. Recommendation based on inconsistent or limited-quality patient-oriented evidence.
- C. Recommendation based on consensus, opinion, case studies, or disease-oriented evidence.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline has been developed in accordance with the American Academy of Dermatology (AAD)/AAD Association *Administrative Regulations for Evidence-based Clinical Practice Guidelines* (version approved May 2010), which includes the opportunity for review and comment by the entire AAD membership and final review and approval by the AAD Board of Directors.

Evidence Supporting the Recommendations

References Supporting the Recommendations

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate prevention of disease flares and use of adjunctive therapies and approaches in patients with atopic dermatitis (AD)

Potential Harms

- One study recorded a higher rate of viral and respiratory tract infections and another found increased ear, nose, and throat symptoms in patients who used topical corticosteroids (TCS). Another long-term safety study of up to 44 weeks of intermittent treatment noted abnormal cosyntropin stimulation testing in 2 of 44 subjects.
- Side effects for proactive topical calcineurin inhibitor (TCI) use were mainly application site reactions, and in one study, skin infections and nasopharyngitis occurred, but these side effects were also seen with the vehicle. Given the current black box warning against continuous TCI use, it seems prudent to apply them intermittently to minimize any potential long-term risks.

Qualifying Statements

Qualifying Statements

- Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be interpreted as setting a standard of care or be deemed inclusive of all proper methods of care nor exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient, and the known variability and biologic behavior of the disease. This guideline reflects the best available data at the time the guideline was prepared. The results of future studies may require revisions to the recommendations in this guideline to reflect new data.
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) or National Institutes of Health (NIH).
- In review of the currently available highest level of evidence, the expert work group acknowledges that while multiple studies have been performed on prevention of flares and the use of adjunctive therapies and approaches, much has yet to be learned.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Sidbury R, Tom WL, Bergman JN, Cooper KD, Silverman RA, Berger TG, Chamlin SL, Cohen DE, Cordoro KM, Davis DM, Feldman SR, Hanifin JM, Krol A, Margolis DJ, Paller AS, Schwarzenberger K, Simpson EL, Williams HC, Elmetts CA, Block J, Harrod CG, Smith Begolka W, Eichenfield LF. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. J Am Acad Dermatol. 2014 Dec;71(6):1218-33. [157 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

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Guideline Developer(s)

American Academy of Dermatology - Medical Specialty Society

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Guideline Committee

Atopic Dermatitis Work Group

Composition of Group That Authored the Guideline

Work Group Members: Robert Sidbury, MD (*Co-chair*); Wynnis L. Tom, MD; James N. Bergman, MD; Kevin D. Cooper, MD; Robert A. Silverman, MD; Timothy G. Berger, MD; Sarah L. Chamlin, MD, MSCI; David E. Cohen, MD; Kelly M. Cordoro, MD; Dawn M. Davis, MD; Steven R. Feldman, MD, PhD; Jon M. Hanifin, MD; Alfons Krol, MD; David J. Margolis, MD, PhD; Amy S. Paller, MD; Kathryn Schwarzenberger, MD; Eric L. Simpson, MD; Hywel C. Williams, DSc; Craig A. Elmetts, MD; Julie Block, BA; Christopher G. Harrod, MS; Wendy Smith Begolka, MBS; Lawrence F. Eichenfield, MD (*Co-chair*)

Financial Disclosures/Conflicts of Interest

Work group members completed a disclosure of interests that was updated and reviewed for potential relevant conflicts of interest throughout guideline development. If a potential conflict was noted, the work group member recused him or herself from discussion and drafting of recommendations pertinent to the topic area of the disclosed interest.

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The below information represents the authors identified relationships with industry that are relevant to the guideline. Relevant relationships requiring recusal for drafting of guideline recommendations and content were not noted for this section. The management of conflict of interest for this guideline complies with the Council of Medical Specialty Societies' *Code of Interactions with Companies*.

Wynnis L. Tom, MD, served as an investigator for Anacor, receiving no compensation.

James N. Bergman, MD, had other relationships with Pediapharm, receiving honoraria, and served as a consultant for Pierre-Fabre, receiving honoraria.

Robert A. Silverman, MD, served as a speaker for Galderma and Promius, receiving honoraria.

Sarah L. Chamlin, MD, MSCI, served on the advisory boards for Anacor, Galderma, Promius, and Valeant, receiving honoraria.

David E. Cohen, MD, served on the advisory boards and as a consultant for Ferndale Labs, Galderma, and Onset, receiving honoraria; served on the board of directors and as a consultant for Brickell Biotechnology and Topica, receiving honoraria, stock, and stock options; and was a consultant for Dermira and Dr Tatoff, receiving honoraria and stock options.

Steven R. Feldman, MD, PhD, served on the advisory boards for Amgen, Doak, Galderma, Pfizer, Pharmaderm, Skin Medica, and Stiefel, receiving honoraria; was a consultant for Abbott, Astellas, Caremark, Coria, Gerson Lehrman, Kikaku, Leo Pharma, Medicis, Merck, Merz, Novan, Peplin, and Pfizer, receiving honoraria, and Celgene, HanAll, and Novartis, receiving other financial benefits; was a speaker for Abbott, Amgen, Astellas, Centocor, Dermatology Foundation, Galderma, Leo Pharma, Novartis, Pharmaderm, Sanofi-Aventis, Stiefel, and Taro, receiving honoraria; served as a stockholder and founder for Causa Technologies and Medical Quality Enhancement Corporation, receiving stock; served as an investigator for Abbott, Amgen, Anacor, Astellas, Basilea, Celgene, Centocor, Galderma, Medicis, Skin Medica, and Steifel, receiving grants, and Suncare Research, receiving honoraria; and had other relationships with Informa, UptoDate, and Xlibris, receiving royalty, and Medscape receiving honoraria. Dr Feldman recused himself for the drafting of guideline recommendations related to phototherapy.

Jon M. Hanifin, MD, served on the advisory board for Chugai Pharma USA, receiving honoraria; was a consultant for GlaxoSmithKline, Merck Elocon Advisory Board, Otsuka Pharma, Pfizer, and Valeant Elidel Advisory Board, receiving honoraria; and served as an investigator for Asubio and Merck Sharp & Dohme, receiving grants.

Alfons Krol, MD, served as an investigator for Pierre-Fabre, receiving grants.

Amy S. Paller, MS, MD, served as a consultant to Anacor, Galderma, Leo Pharma, Promius, Sanofi/Regeneron, and TopMD, receiving honoraria; and was an investigator for Astellas, Galderma, Leo Pharma, and TopMD, receiving no compensation.

Eric L. Simpson, MD, served as a consultant for Asubio, Brickell Biotech, Galderma, Medicis, Panmira Pharmaceuticals, and Regeneron, and a speaker for Centocor and Galderma, receiving honoraria; and was an investigator for Amgen, Celgene, Galderma and Regeneron, receiving other financial benefits.

Craig A. Elms, MD, served on a data safety monitoring board for Astellas, receiving honoraria.

Lawrence F. Eichenfield, MD, served as a consultant for Anacor and Bayer, receiving honoraria, and TopMD, receiving stock options; was a consultant and speaker for Galderma, receiving honoraria; served as a consultant, speaker, and member of the advisory board for Medicis/Valeant, receiving honoraria; and was an investigator for Anacor and Astellas, receiving no compensation.

Robert Sidbury, MD, Timothy M. Berger, MD, Kevin D. Cooper, MD, Kelly M. Cordoro, MD, Dawn M. Davis, MD, David J. Margolis, MD, PhD, Kathryn Schwarzenberger, MD, Hywel C. Williams, DSc, Julie Block, BA, Christopher G. Harrod, MS, and Wendy Smith Begolka, MBS, have no relevant relationships to disclose.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Hanifin JM, Cooper KD, Ho VC, Kang S, Krafchik BR, Margolis DJ, Schachner LA, Sidbury R, Whitmore SE, Sieck CK, Van Voorhees AS. Guidelines of care for atopic dermatitis. J Am Acad Dermatol. 2004 Mar;50(3):391-404. [212 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [American Academy of Dermatology \(AAD\) Web site](#) .

Availability of Companion Documents

The following is available:

- American Academy of Dermatology (AAD) guideline development process. Schaumburg (IL): American Academy of Dermatology (AAD).

Patient Resources

The following is available:

- Atopic dermatitis. For the public. Schaumburg (IL): American Academy of Dermatology (AAD). Available from the [American Academy of Dermatology \(AAD\) Web site](#) .

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NGC Status

This NGC summary was completed by ECRI on April 19, 2004. The information was verified by the guideline developer on May 19, 2004. This summary was updated by ECRI on March 15, 2005 following release of a public health advisory from the U.S. Food and Drug Administration regarding the use of Elidel. This summary was updated by ECRI on January 31, 2006, following release of a public health advisory from the U.S. Food and Drug Administration regarding the use of Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus). This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on CellCept (mycophenolate mofetil). This summary was updated by ECRI Institute on July 8, 2008, following the updated U.S. Food and Drug Administration (FDA) advisory on CellCept (mycophenolate mofetil) and Myfortic (mycophenolate acid). This summary was updated by ECRI Institute on February 19, 2009, following the U.S. Food and Drug Administration (FDA) advisory on CellCept (mycophenolate mofetil). This summary was updated by ECRI Institute on March 26, 2009, following the updated FDA advisory on CellCept and Myfortic. This summary was updated by ECRI Institute on August 18, 2009, following the revised FDA advisory on CellCept (mycophenolate mofetil). This summary was updated by ECRI Institute on August 24, 2009, following the revised FDA advisory on CellCept (mycophenolate mofetil). This summary was updated by ECRI Institute on September 11, 2009, following the revised FDA advisory on Myfortic (mycophenolic acid). This summary was updated by ECRI Institute on July 14, 2015. The updated information was verified by the guideline developer on November 6, 2015.

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